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Characterization of bi-ventricular coronary flow reserve and remodeling in mice with pressure overload cardiac hypertrophy

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Objectives: Coronary microcirculation is critically involved in the cardiac adaption to pressure overload. Both clinical and high frequency ultrasound systems have been used to measure coronary flow in mice, but limited to the left coronary artery (LCA). The advent of high frequency Doppler flow imaging makes it possible to visualize the septal (SCA) and right (RCA) coronary arteries in a mouse model of pressure overload induced by transverse aortic constriction (TAC). Here, using high frequency Doppler ultrasound, we aimed to evaluate the flow patterns of the LCA, SCA and RCA in mice with TAC, and associate the flow parameters with corresponding structural and functional changes of both ventricles.
Methods: Forty-eight male C57BL/6J mice were subjected to TAC or corresponding sham operation. At 2 and 8 weeks post surgery, Doppler flow spectra from the three coronary arteries, together with echocardiographic structural and functional parameters of the left and right ventricles, were measured. Histology was performed to evaluate cardiomyocyte size and neoangiogenesis in both ventricles.
Results: In sham-operated mice, the LCA and SCA both showed low flow waveforms during systole and dominantly higher flow waveforms during diastole. The RCA exhibited generally lower flow velocity, with similar systolic and diastolic waveforms. TAC significantly increased the systolic flow velocities of all coronary arteries, but enhanced the flow mainly in the LCA and SCA. In the left ventricle, compared with sham-operated animals, coronary flow reserve (CFR) was partially preserved at 2 weeks post TAC (2.37±0.20 vs. 1.70±0.22 for LCA, $P<0.05$; 2.12±0.16 vs. 2.19±0.23 for SCA, $P>0.05$), but decreased at 8 weeks (2.48±0.23 vs. 1.75±0.17 for LCA, $P<0.05$; 2.34±0.22 vs. 1.58±0.12 for SCA, $P<0.05$), consistent with increased angiogenesis and negligibly changed systolic function at 2 weeks after TAC, but prominently blunted angiogenesis and systolic function at 8 weeks after TAC. In contrast, no significant change was found in the CFR, structure or function of the right ventricle.
Conclusions: This study has established an echocardiographic protocol for assessment of the flow pattern in three principal coronary arteries in mice and demonstrated the difference among three vessels and bi-ventricular remodeling at baseline and in pressure overload. Under TAC, it's elevated ventricular pressure rather than coronary perfusion pressure, causes structural and functional change as demonstrated in the RCA and right ventricle. The difference in the associating pattern of the coronary flow dynamics with the myocardial structure and function between the left and right ventricles facing distinctive loading conditions provides further insights into pressure overload induced ventricular remodeling.

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To study the diagnostic value of matrix metalloproteinase -9 in ST segment elevation myocardial infarction by ROC curve

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Objectives: Matrix metalloproteinase-9 (MMP-9) is regarded as a biomarker of plaque rupture or vulnerability and is elevate in patients with acute coronary syndrome (ACS). The aim of the present study was to evaluate the diagnostic value of MMP-9 in ST segment elevation myocardial infarction (STEMI) by using receiver operating characteristic (ROC) curve and compared with creatine kinase-MB (CK-MB).
Methods: From September 2011 to February 2012, according to the "Chinese guideline of diagnosis and treatment: of acute ST-segment elevation myocardial infarction (STEMI) " (2010) established by the expert group in Chinese Society of Cardiology of Chinese Medical Association and Editorial Board of Chinese Journal of Cardiology, we selected 55 cases of STEMI in Coronary Care Unit (CCU) at the Heart Center of The First Affiliated Hospital of Xinjiang Medical University as our STEMI experimental group. Meanwhile, 50 cases in general ward at the Heart Center with symptoms of atypical chest pain but no abnormality of left and right coronary arteries in coronary angiography were selected as our control group. As the STEMI patients' myocardial infarction symptom occurred, we made the experiment based on the following different length of time after the symptom onset respectively: t≤4h (called Group ≤4 h), 4<t≤8h (called Group 4h<t≤8h), 8h<t≤12h (called Group 8h<t≤12h), 12h<t≤24h (called Group 12h<t≤24h), 24h<t≤48h (called Group 24h<t≤48h). The experiment included the measuring to the expression levels of MMP-9 in the plasma and the creatine kinase-MB (CK-MB); as well as using ROC curve to evaluate the diagnostic value of MMP-9 and CK-MB for STEMI.
Results: In STEMI patients, the levels of MMP-9 were 1.53±0.90 μg/ml (t≤4h, $P<0.001$), 1.49±0.88μg/ml (4<t≤8h, $P<0.001$), 1.65±0.79 μg/ml (8h<t≤12h, $P<0.001$), 1.89±0.72μg/ml (12h<t≤24h, $P<0.001$), 1.81±0.71μg/ml (24h<t≤48h, $P<0.001$) all significantly higher than the control group (0.20±0.02μg/ml). In addition to the ≤4 h group (48.69±58.37U/L, $P=0.131$), the levels of CK-MB in STEMI patients were 114.06±81.55 U/L (4<t≤8h, $P<0.001$), 143.96±127.05 U/L (8h<t≤12h, $P<0.001$), 123.79±126.82 U/L (12h<t≤24h, $P<0.001$), 74.33±140.62 U/L (24h<t≤48h, $P=0.003$) significantly higher than the control group (11.62±4.09 U/L). On ROC curve analysis, areas under the curve (AUC) of STEMI were 0.987, 0.949, 0.995, 0.989 and 0.977 for MMP-9; Youden index were 0.880, 0.869, 0.962, 0.944 and 0.944, respectively. The AUC of CK-MB were 0.852, 0.967, 0.976, 0.955 and 0.870, and Youden index were 0.642, 0.855, 0.927, 0.873 and 0.687 in STEMI, respectively.
Conclusions: MMP-9 level was elevated earlier than CK-MB and had a higher diagnostic value for early STEMI and for late STEMI.

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Macrophage migration inhibitory factor in predicting short- and long-term major adverse cardiovascular events in patients with ST-segment elevation myocardial infarction

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Objectives: Macrophage migration inhibitory factor (MIF) play an important role in plaque development and stability, serve as a marker of early acute coronary syndrome (ACS) and of plaque instability. In the present study we aimed to assess the capacity of MIF to predict short- and long-term major adverse cardiovascular events (MACE) in ST-segment elevation myocardial infarction (STEMI) patients.
Methods: Prospectively consecutive included 90 patients admitted to coronary care unit (CCU), The First Teaching & Affiliated Hospital, Xinjiang Medical University, with a first STEMI from September 2011 to May 2013. Meanwhile, we recruited 44 patients with chronic stable angina (CSA) from the general ward of Heart center, and 44 healthy consecutive volunteers from the Medical Examination Center. MIF plasma concentrations were measured in 90 STEMI patients, 44 CSA patients and 44 healthy consecutive volunteers on admission. The endpoints of the study was MACE, The median follow-up was 18 months.
Results: The level of admission MIF was significantly higher in STEMI patients (91.99 (70.64-121.05) ng/mL) than CSA patients (52.25 (41.04-70.71) ng/mL, $P<0.001$) and healthy controls (18.44 (13.39-30.17) ng/mL, $P<0.001$). During hospitalization, 10 MACE occurred, the independent predictors of in-hospital MACE were: admission MIF (OR 1.00 95% CI 1.00-1.00, $P=0.038$, per each ng increase), admission greatinine (OR 1.04 95% CI 1.01-1.08, $P=0.006$, per each umol increase) and AUC CK-MB (OR 1.00 95% CI 1.00-1.00, $P=0.006$, per each U increase). The area under the receiver operating characteristic (ROC) curve with MIF used to predict in-hospital MACE was 0.77 (95% CI 0.64-0.89). A cut-off point of 104.38ng/mL showed a sensitivity of 70% and specificity of 66% for prediction of in-hospital MACE. During a median follow-up of 18 months, 9 MACE occurred, the independent predictors of long-term MACE were: admission MIF (HR 1.04 95% CI 1.01-1.07, $P=0.019$, per each ng increase), admission greatinine (HR 1.34 95% CI 1.12-1.60, $P=0.002$, per each mmol increase). The area under the ROC curve with MIF used to predict long-term MACE was 0.78 (95% CI 0.66-0.89), the cut-off value for the prediction of long-term MACE was 104.38ng/mL. In patients with MIF≥104.38ng/mL, the crude MACE rate was significantly higher compared to patients with MIF<104.38ng/mL (21% (6/29) vs. 6% (3/53), $P=0.04$) .
Conclusions: Our experimental and clinical findings indicate that a single MIF assay at admission could be a useful biomarker for early prediction of in-hospital and long-term MACE of patients with STEMI.

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Catheter-based renal denervation lowers blood pressure in hypertensive mini-pigs

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Objectives: Although catheter-based renal denervation (RDN) shows a potent benefit in the treatment of resistant hypertension, there is a considerable controversy still exists on some aspects. The differentiation of individual-specific or model-specific response to RDN may be attributed to the different mechanisms involved in the maintenance of hypertension. This study was performed to investigate the effect of RDN on blood pressure (BP) and renal function in spontaneous hypertensive mini-pigs.
Methods: 16 spontaneous mini-pigs were divided into three groups: sham group (n=6), Sniper RDN group (n=5), and Symplicity RDN group (n=5). After measurement of the baseline BP and renal function, the bilateral RDN was performed using the Sniper (APT Medical Inc., Shenzhen, China) and Symplicity (Medtronic Inc., Minneapolis, MN) system, respectively. 12 weeks after the procedure, BP and renal function were measured, renal arteries were histological analyzed, and the renal arterial angiography was performed.
Results: The three groups of mini-pigs had similar systolic (sham 187.8±9.6, Sniper 186.0±13.3 Symplicity 169.4±7.7 mmHg, $P>0.05$) and diastolic (sham 136.8±6.5, Sniper 134.0±9.7 Symplicity 126.0±6.2 mmHg, $P>0.05$) BP at baseline. 12 weeks after the RDN procedure, the systolic (sham 192.4±10.5, Sniper 113.8±14.4, Symplicity 115.6±11.1 mmHg, sham vs. Sniper $P<0.01$, sham vs. Symplicity $P<0.01$) and diastolic (sham 141.2±5.9, Sniper 79.4±11.7, Symplicity 79.8±12.1 mmHg, sham vs. Sniper $P<0.01$, sham vs. Symplicity $P<0.01$) BP were significantly lowered